

Remarks

The Final Office Action dated October 23, 2002 has been carefully reviewed and the foregoing remarks are made in response thereto. In view of the following remarks, Applicant respectfully requests reconsideration and reexamination of this application and the timely allowance of the pending claims.

Summary of Final Office Action

1. Claims 18 to 24 were rejected under 35 U.S.C. 103(a) as being unpatentable over Graham *et al.* (U.S. Patent 6,127,120) in view of Hacia *et al.* (U.S. Patent 6,013,449), McGall *et al.* (U.S. Patent 6,156,501) and Fodor *et al.* (U.S. Patent 5,800,992).

2. Claims 25 to 28 were found to be free of the prior art.

Remarks

Applicant appreciates the efforts of the examiner in furthering the prosecution of the present application by discussing the merits of the claim rejections with Applicant's agent on multiple occasions. In an effort to further expedite the prosecution, Applicant hereby requests an interview with the Examiner following consideration of the arguments in the present response.

Rejection under 35 U.S.C. 103

Claims 18 to 24 were rejected under 35 U.S.C. 103 purportedly because the claimed invention is not patentable over Graham *et al.* (U.S. Patent 6,127,120) in view of Hacia *et al.* (U.S. Patent 6,013,449), McGall *et al.* (U.S. Patent 6,156,501) and Fodor *et al.* (U.S. Patent 5,800,992).

The rejected claims provide the feature that the reusable array is stripped of hybridized nucleic acids between steps or between experiments by washing with an acidic solution of pH 1 to 2 (*i.e.*, conditions under which the nucleic acids are protonated). The Examiner purports that the disclosure in Fodor *et al.* relating to modifications in pH indicate the need for the skilled artisan to adjust the pH conditions based on substrate chemistry. Applicant brings to the attention of the Examiner that "obvious to try" is not the standard under 35 U.S.C. 103 for determining obviousness (see M.P.E.P. 2145 X.B). The cited reference gives no indication of which parameters are critical and no direction as to which of the many combinations are likely to be successful.

Applicant also submits that the skilled artisan would not have been motivated to adjust the pH level to those disclosed in the claimed method (*i.e.*, pH 1 to 2). This reference discloses that substrate

reuse should employ mild conditions and neutral pH if recycling is desired (column 56, lines 2-7) and makes no mention of an acidic pH to the level claimed by Applicant. The skilled artisan would not have been motivated to employ a buffer with pH of 1 to 2 in the claimed method given the state of the art as of the filing date. Such acidic conditions would have been expected to degrade the oligonucleotides on the array, rendering it useless. The claimed method therefore proceeds contrary to accepted wisdom and is thus evidence of non-obviousness (see M.P.E.P. 2145 X.D.3).

With regard to Graham *et al.*, Applicant brings to the attention of the Examiner that the cited reference discloses that the array can be prepared for reuse by removal of mRNA by treatment with RNase or alkali (column 31, lines 60 to 66) and makes no reference to acidic conditions for stripping an array for reuse. Applicants submit that the disclosure of basic or enzymatic washing conditions by Graham *et al.* clearly teaches away from the claimed method wherein strongly acidic washing conditions are employed to remove the hybridized nucleic acids from the array.

With regard to McGall *et al.*, the Examiner indicates that this reference purportedly discloses the use of modified oligonucleotides on arrays for reuse citing column 9, lines 37 to 39. Applicant submits that the cited passages make no mention of reuse of an array but rather only discuss "fabrication or subsequent use" (see column 9, line 40). A word search of the cited reference reveals that the term "reuse" is not disclosed anywhere in the specification nor claims. Applicant submits that there is no disclosure in the cited reference that would lead the skilled artisan to believe that the disclosed arrays could be reused.

Finally, Applicant submits that in the absence of either Fodor *et al.*, Graham *et al.* or McGall *et al.* there is no motivation in the remaining cited references to modify their teachings to produce the claimed invention. Furthermore, none of the cited references, either alone or in combination, teach or suggest all of the features of the claimed methods for identifying nucleic acid sequence differences between target and reference molecules using highly acid-resistant reusable oligonucleotide arrays, nor do they render Applicant's claimed method obvious.

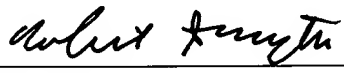
Conclusion

Applicant respectfully requests reconsideration and the timely allowance of the pending claims. A favorable action is awaited. Should the Examiner find that an interview would be helpful to further prosecution of this application, he is invited to telephone the undersigned at their convenience.

Except for issue fees payable under 37 C.F.R. 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-0310. This paragraph is intended to be a **Constructive Petition for Extension of Time** in accordance with 37 C.F.R. 1.136(a)(3).

Dated: **November 24, 2003**
Morgan, Lewis & Bockius LLP
Customer No. **09629**
1111 Pennsylvania Avenue, N.W.
Washington, D.C. 20004
202-739-3000

Respectfully submitted
Morgan, Lewis & Bockius LLP



Robert Smyth
Registration No. 50,801